ACOUSTIC HEMOSTASIS AND HEMORRHAGE CONTROL IN COMBAT CASUALTY CARE

Lawrence Crum, Marilee Andrew, Stephen Carter, Francesco Curra, Peter Kaczkowski, Steve Kargl, Andrew Brayman, and Shahram Vaezy

Center for Industrial and Medical Ultrasound
Applied Physics Laboratory
University of Washington, Seattle, WA 98105
*lac@apl.washington.edu

and

Henry Bass, Frank Barber*, Charles Church, and Sara Davis

National Center for Physical Acoustics
University of Mississippi
1 Coliseum Drive
University, MS 38677-1848

ABSTRACT

High Intensity Focused Ultrasound (HIFU) is a new treatment modality that shows great promise for hemorrhage control and hemostasis in trauma applications. This paper discusses our multi-center, multi-disciplinary effort to develop intraoperative and transcutaneous, ultrasound-image-guided, acoustic hemostasis treatment systems for use in combat casualty care.

1. INTRODUCTION

Since the Crimean War, the mortality rate for battlefield injuries has improved only marginally [Zajtchuk and Sullivan, 1995; Bellamy, 1984]. Although there has been some reduction in mortality for those combatants reaching the medical system, there has been little improvement for those who do not. The principal reason for this lack of improvement is that for severe wounds, there is a limited time in which medical care can be effective. The so-called "golden hour" may even be an exaggeration in the combat casualty care environment. Indeed, Zajtchuk and Sullivan [1995] have shown that ~67% of the mortality occurs within the first 10 minutes after injury; an additional 28% die within an hour, and only ~5% of the deaths occur after the first hour. These data suggest that immediate medical care is required if significant reductions in mortality are to be expected. Thus, a concept of the modern battlefield is to bring advanced technology to the battlefield, rather than to evacuate the wounded soldier to a technically sophisticated medical care unit. An important aspect of medical treatment is to diagnose quickly and correctly the life-threatening condition so that remedial therapy can address this condition. We are developing a self-contained technology to utilize ultrasound to image a site of bleeding and then to apply High Intensity Focused Ultrasound (HIFU) to this site to induce cauterization and to terminate/control the bleeding. We call this approach "Image-guided Acoustic Hemostasis".

2. METHODS AND RESULTS

There are three major components of a successful effort to use Image-guided HIFU therapy to control bleeding: (1) to detect that bleeding has occurred, (2) to target the bleeding site, and (3) to apply sufficient levels of HIFU to induce hemostasis. We examine each of these tasks individually.

2.1 Detection of bleeding

Current diagnostic ultrasound imaging systems range in size from a small refrigerator to a shoebox, and in cost from on the order of $300k to less than $10k. We were involved in the development of a small portable unit [Hwang et al., 1998] that has had much success in emergency care [Funk, 2004]. We have used these portable "hand-held" devices, such as the SonoSite 180, for bleeding detection in our laboratory. This device, and/or similar versions, has Doppler imaging capabilities. Doppler can be used in a "color-flow mode" to detect a site of bleeding for which a major vessel is breached and significant flow is occurring. Doppler can also be used in a "power Doppler" mode in which any form of fluid motion is detected. In this mode, we often look for sites that show a lack of perfusion, indicating that a particular

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE **00 DEC 2004**	2. REPORT TYPE **N/A**	3. DATES COVERED **-**

4. TITLE AND SUBTITLE **Acoustic Hemostasis And Hemorrhage Control In Combat Casualty Care**	5a. CONTRACT NUMBER 5b. GRANT NUMBER 5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	5d. PROJECT NUMBER 5e. TASK NUMBER 5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) **Center for Industrial and Medical Ultrasound Applied Physics Laboratory University of Washington, Seattle, WA 98105; National Center for Physical Acoustics University of Mississippi 1 Coliseum Drive University, MS 38677-1848**	8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S) 11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES
See also ADM001736, Proceedings for the Army Science Conference (24th) Held on 29 November - 2 December 2005 in Orlando, Florida., The original document contains color images.

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT **unclassified**	b. ABSTRACT **unclassified**	c. THIS PAGE **unclassified**	**UU**	**8**	

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std Z39-18

region of tissue is ischemic and showing little or no perfusion to this area. Bleeding can also be detected by searching for hypoechoic as well as hyperechoic regions. As a pool of blood ages, it can change from hypoechoic to hyperechoic. We have learned that a rapid scan of the pouch of Douglas or Morison's pouch can indicate if internal bleeding is occurring.

Fig. 1 shows an example of the use of Color Doppler to detect bleeding in a lacerated femoral artery of a pig, while Fig. 2 shows a region of a porcine kidney that is ischemic and shows a lack of perfusion to a particular region. In this latter case, Color Power Doppler was used to examine a region of the kidney in which 2 major vessels supplying blood to a particular region of interest was damaged, thus starving that particular region of perfusion.

Fig. 1. The use of diagnostic ultrasound devices that have Color Flow Doppler capability can detect high-flow rate bleeds such as this one in the femoral artery of a pig.

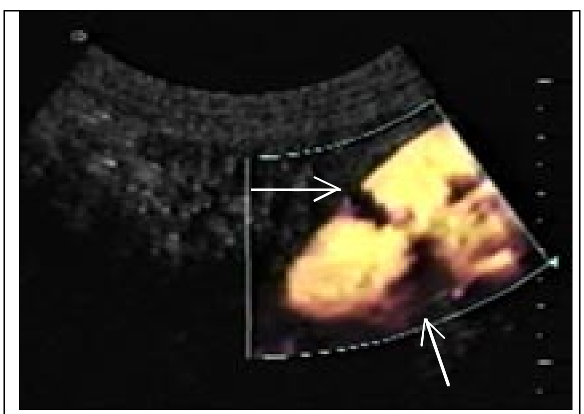

Fig. 2. The use of diagnostic ultrasound devices that have color power Doppler capability can detect regions that are ischemic such as this damage to the vessels in the kidney of a pig [after Schmiedl et al., 1999].

2.2. Targeting of the bleeding site

Once a bleeding site, such as that shown in Fig. 1 is identified, the next task is to ensure that the HIFU to be delivered to induce hemostasis is directed exclusively to that site; accordingly, it is important to have some targeting system or approach that ensures that the powerful HIFU beam is accurately directed. We have discovered that low-level HIFU induces spontaneous out-gassing of the tissue being insonified and permits us to identify in real time if our therapy beam is properly placed [Vaezy, et al., 2001]. This out-gassing results in a hyperechoic region in the ultrasound image, thus permitting one to identify the location of focus of the therapy beam. Shown in Fig. 3 is an example of this hyperechoic region during HIFU exposure to a porcine liver.

Fig. 3. Illustration of the use of a hyperechoic region in the ultrasound image to provide HIFU targeting. The arrow indicates that the HIFU and imaging beams are both engaged; the circle encloses a hyperechoic spot that probably results from tissue out-gassing. If a bleeding site was located in the ultrasound image, the hyperechoic spot, indicating the location of the focus of the HIFU beam, would be directed confocal with the site of bleeding.

2.3. The application of therapy

Although the *present* implementation of Image-guided Acoustic Hemostasis seems better suited to intra-operative applications (the major thrust of our present research), we have made significant progress and have high expectations that the necessary targeting and therapy-guidance capabilities can be developed over the next several years to permit transcutaneous therapeutics to be used by a properly trained medic. The main cause of death from both military and civilian trauma is blood loss [Anderson,

2002; Zajtchuk and Sullivan, 1995]; there are innumerable applications wherein an appropriately and well-targeted application of HIFU could save lives by effecting hemostasis, especially if it could be used in the remote and unsanitary conditions where the military needs are greatest. Such a system might be deployed locally under the direction of a physician, or used as part of current efforts to deliver care remotely *via* telerobotic surgery. Thus, we are currently investigating the technology and the biophysical mechanisms through which ultrasound can be used for determining a site of bleeding, through which it can be used to target that site, and finally through which it can be used to induce hemostasis, or at least, hemorrhage control. As indicated above, the technology currently exists in COTS hardware that permits bleeding detection and localization to be performed with portable, light-weight instruments that are currently being deployed in forward echelons of combat casualty care. The major challenge is whether appropriately directly HIFU can be used to induce hemostasis, or at least retard bleeding rates to an acceptable level. We turn now to our efforts in developing the technology of bleeding control.

We have followed two approaches to the use of HIFU for acoustic hemostasis. As a first step, we have constructed intraoperative acoustic hemostasis devices that can be used to treat visible bleeding [Cornejo et al., 2004; Crum et al., 1998; Curra et al., 2003; Martin et al., 1998; 1999, 2003; Vaezy et al., 1997; 1998a; 1998b; 1999].

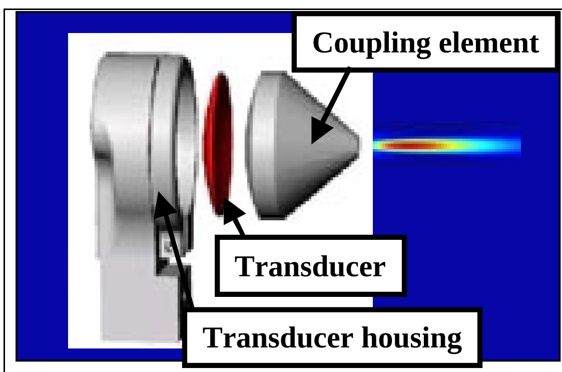

Fig. 4. The components of an intraoperative acoustic hemostasis device. One of the more important components of this device is the coupling element that transfers the acoustic energy from the transducer to the tissue. Various embodiments are used, including metal cones and biocompatible hydrogels.

This approach has enable us to learn much about the basic physics and biology of HIFU-induced hemostasis and has permitted us to advance to image-guided approaches with more confidence. An example of an intraoperative acoustic hemostasis device is show in Fig. 4.

The (time-averaged) intensity levels used in diagnostic ultrasound imaging are quite low when compared with those used for therapy—say, 300 mW/cm^2 for imaging and 3000 W/cm^2 when used for therapy, a difference of 4 orders of magnitude. Accordingly, different transducer technologies are used for the delivery of these two different types of ultrasound energy [Kaczkowski, et al., 2003]. Actually, one could probably use the same transducer array to do both, but this is a level of complexity that we have not yet achieved. In our current system, we have separated the imaging and therapy transducers, although they are tied together mechanically so that coplanar applications can be achieved. Shown in Fig. 5 is an example of one of our combined imaging/therapy systems.

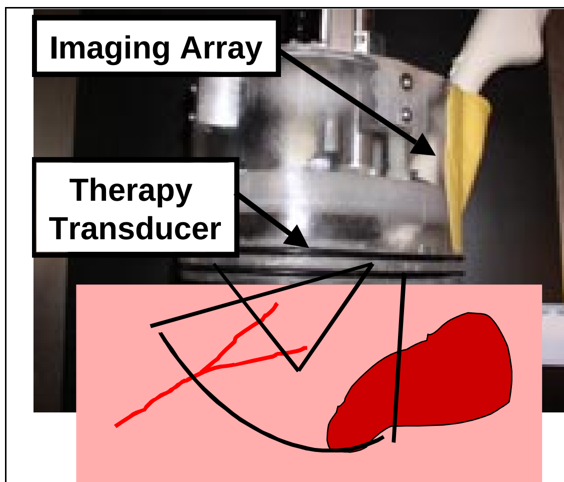

Fig. 5. This photograph shows an image-guided therapy system that uses a Philips C9-5 imaging transducer combined with a single-focus HIFU therapy transducer. With the mechanically -coupled system used, the transducers are coplanar, which permits real-time image guidance of the therapy.

In the system shown in Fig. 5, the HIFU focus can be mechanically steered along the transducer axis, which enables a bleeding vessel to be identified with the imaging transducer in the imaging plane, and then targeted with the therapy transducer so that a specific vessel or bleeding region can be treated.

3. RESULTS

We have been successful in demonstrating hemostasis in two different approaches:

- Using an intraoperative HIFU transducer, we have been able to treat visible bleeding sites and induce hemostasis [Martin et al., 1998; 1999; 2003; Vaezy et al., 1997; 1998a; 1999] and

- Using an image-guided HIFU therapy system, we have been able to successfully treat occult bleeding and to induce hemostasis [Cornejo et al., 2004; Vaezy et al., 1998b].

3.1. Intraoperative acoustic hemostasis

We show in Fig. 6 an example of the application of an intraoperative acoustic hemostasis device to the treatment of bleeding in a transected porcine liver. Organs such as the liver and the spleen are highly perfused organs and consequently, when damaged, are sites of major internal bleeding. Currently popular hemostasis devices, such as electrocautery, are marginally successful in treating bleeding in such organs. In the example shown in Fig. 6, we demonstrate how our version of an acoustic hemostasis device can rapidly induce cauterization to some depth, because the acoustic field can penetrate into the tissue, thus providing "volume cauterization", unlike electrocautery, which can produce only surface cauterization.

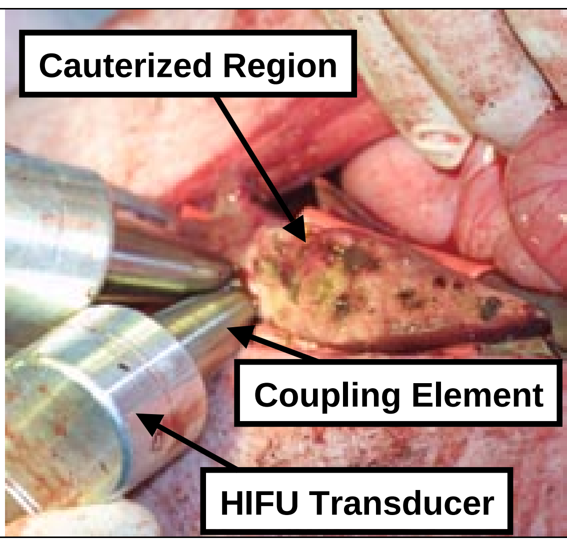

Fig. 6. An example of the use of an intraoperative HIFU device for the induction of acoustic hemostasis of visible bleeding. In this case, a portion of the liver of a pig was transected, and the HIFU applied directly to the site of bleeding in the liver.

3.2. Image-guided transcutaneous acoustic hemostasis

The most attractive use of image-guided acoustic hemostasis is the far forward echelons of combat casualty care in which exsanguination can typically occur within a few minutes of injury, and before the combatant can reach a higher level of medical care. For those injured who reach the operating room, very high rates of survival are now occurring [Holcomb et al., 1999a; 1999b]. Although constructing a device that would be used in these far forward echelons presents a major challenge, we believe that we have demonstrated many important components of this goal and with the appropriate dedication of effort and resources, such a device could be constructed, tested and utilized.

Our approach would probably follow that of Asensio [Asensio, 1990; Asensio et al., 2000; 2001; 2003a; 2003b; 2004a; 2004b] who has published extensively on the topic of advanced trauma care, particularly to Grades IV and V injuries to the liver. This form of trauma is fatal in approximately 50% of cases and proceeds so rapidly that it duplicates similar advanced trauma under battlefield conditions [Beal, 1990; Beal et al., 1996; Beitsch, 1994; Hoyt et al., 1994; Patcher and Hofsetter, 1995; Sauaia et al., 1995; Shackford et al., 1993]. Asensio's approach is to perform rapid embolization of the vessels that are supplying the sites of hemorrhage. This embolization must be done under fluoroscopy, and normally in the "cath lab". Since most patients suffering severe trauma are first treated in the operating room, a major cause of mortality is the lack of proactive care in the transit from the operating room to the cath lab.

We have developed a technological approach that we believe will enable trauma surgeons such as Asensio to perform an effective vessel occlusion while in the operating room. Our system is similar to that shown in Fig. 5, in which we have constructed an imaging array tied mechanically to a therapy transducer that provides sufficient levels of HIFU so as to rapidly induce vessel occlusion.

Our approach, demonstrated successfully in large animal models, thus follows a protocol that we have demonstrated successfully in a number of animal models. This protocol also follows our general approach of bleeding detection, localization, and hemorrhage control. An example of the application of this protocol to a porcine model is shown in Fig. 7.

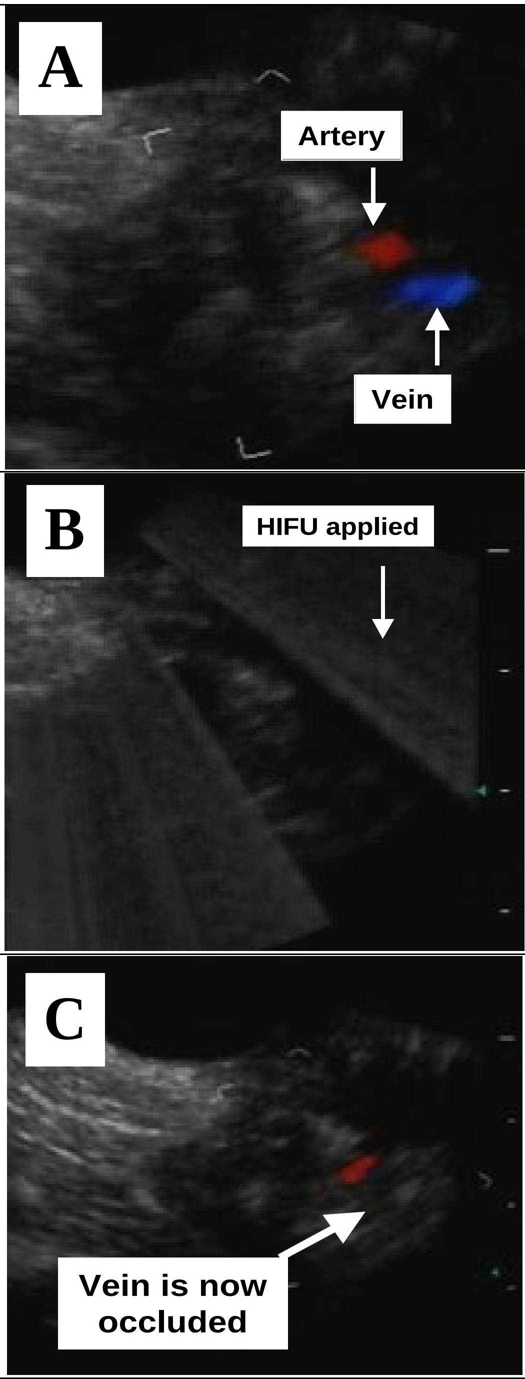

Fig. 7. Demonstration of successful application of image-guided HIFU for vessel occlusion, using a device similar to that shown in Fig. 5. In A, the Doppler imaging system is used to identify a vein that is supplying a region of hemorrhage in a porcine liver; in B, the vessel is targeted and HIFU is applied; in C, rescanning with Doppler, the vein in question shows no flow and thus by implication is occluded. In this manner, rather than treating the entire region of hemorrhage, the vessels supplying the region of bleeding are effectively embolized.

We can express this protocol explicitly as follows:

- Some form of trauma is induced in the liver of a pig,

- the vessels leading to this hemorrhaging area of located with a Doppler ultrasound device,

- HIFU is supplied to these vessels proximal to the site of trauma,

- the flow in these vessels is monitored by color Doppler, and

- HIFU is supplied to these vessels until the color Doppler indicates that total vessel occlusion has occurred.

4. FUTURE PERSPECTIVES

We have demonstrated that image-guided transcutaneous acoustic hemostasis devices can be utilized to identify a site of bleeding, to target it, and with the appropriate application of HIFU therapy, induce hemostasis or at least a comfortable level of hemorrhage control. The devices that we have developed in our laboratory are not yet at a level of technical sophistication that they could be converted into engineering prototypes.

We anticipate that for a device to be attractive to the combat medic, or battalion aide physician, it would need to be lightweight and portable, and require only modest levels of training. Such a device can be envisioned. It would contain the following components:

- A lightweight, handheld imaging system capable of both color flow and color power Doppler, in addition to normal B-scan,

- an annular array for application of the HIFU therapy, so that one could electronically direct the therapy at any depth,

- a simple human interface system that contained artificial intelligence that would seek sites of bleeding and automatically target vessels leading to this site of bleeding, thus permitting rapid and direct deployment of the therapy to an injured combatant.

We show in Fig. 8 an example of such a system.

Fig. 8. Potential configuration of an image-guided, transcutaneous acoustic hemostasis system.

5. CONCLUSIONS

We have made considerable progress in our extensive preliminary studies in laboratory animals and have demonstrated that HIFU can induce hemostasis in a variety of bleeding scenarios. We have also demonstrated that HIFU can be combined with an ultrasound imaging system to perform image-guided acoustic hemostasis of occult bleeding. Further developments of this technology offer promising approaches to critical combat casualty care issues.

ACKNOWLEDGEMENTS

We acknowledge the support of the US Army Medical Research and Material Command.

REFERENCES

Anderson RN. Deaths: leading causes for 2000. Natl Vital Stat Rep 2002; 50: 1-85.

Asensio JA. Exsanguination from penetrating injuries. J Trauma Q 1990; 6: 1-25.

Asensio JA, Ierardi R. Exsanguination. Emerg Care Q 1991; 7: 59-75.

Asensio JA, Hanpeter D, Gomez H, *et al.* Exsanguination. In: Shoemaker WC, Grenvik A, Ayres SM, Holbrook PR (eds). *Textbook of Critical Care*. Philadelphia: WB Saunders, 2000: 437-447.

Asensio JA, McDuffie L, Petrone P, Roldan G, Forno W, Gambaro E, Salim A, Demetriades D, Murry J, Velmahos G, Shoemaker W, Berne TV, Ramicone E, Chan L. Reliable variables in the exsanguinated patient which indicate damage control and predict outcome. Am J Surg 2001; 182: 743-751.

Asensio JA, Roldan G, Petrone P, Rojo E, Tillou A, Kuncir E, Demetriades D, Velmahos G, Murray J, Shoemaker WC, Berne TV, Chan L. Operative management and outcomes in 103 AAST-OIS grades IV and V complex hepatic injuries: Trauma surgeons still need to operate, but angioembolization helps. J Trauma 2003; 54: 647-654.

Asensio JA, Petrone P, O'Shanahan G, Kuncir EJ. Managing exsanguination: What we know about damage control/bailout is not enough. BUMC Proceedings 2003; 16: 294-296.

Asensio JA, Petrone P, Roldan G, Kuncir E, Ramicone E Chan, L. Has evolution in awareness of guidelines for institution of damage control improved outcome in the management of the posttraumatic open abdomen. Arch Surg 2004a; 139: 209-214.

Asensio JA, Petrone P, Kimbrell B, Kuncir E, Ramicone E, Chan L. Prospective study of operative management in 75 hepatic injuries AAST-OIS grades IV-V: Operative intervention and postoperative angioembolization reduces mortality. 2004b; Abstract and personal communication.

Beal SL. Fatal hepatic hemorrhage: An unresolved problem in the management of complex liver injuries. J Trauma 1990; 2: 163.

Beal SL. Liver. In: Ivatury RR, Cayten CG (eds.), *The Textbook of Penetrating Trauma*. William and Wilkins, Baltimore, MD, 1996; Chapter 46, p. 571-588.

Beitsch P. Liver and biliary tract trauma. In: Lopez-Viego MA (ed.), *The Parkland Trauma Handbook*, Mosby, St. Louis, MO, 1994; Chapter 36, p. 279.

Bellamy RF. The causes of death in conventional land warfare: implications for combat casualty care research. Mil Med 1984; 149: 55-62.

Cornejo C, Vaezy S, Jurkovich G, Paun M, Sharar S, Martin R. High intensity ultrasound treatment of blunt abdominal solid organ injury: an animal model. J Trauma 2004; (in press).

Crum L, Bailey M, Kaczkowski P, Makin I, Mourad P, Beach K, Carter S, Schmeidl U, Chandler W, Martin R, Vaezy S, Keilman G, Cleveland R, Roy R: Therapeutic ultrasound: A promising future in clinical medicine. Proc. 16th ICA/135th ASA Meeting, Seattle, WA, 2: 719-720, 1998.

Curra FP , Kargl SG, Crum LA. Parameter space investigation for optimal thermal lesion generation in noninvasive HIFU applications. In: Andrew MA, Crum LA, Vaezy S (eds.) *Proc. 2nd Internat'l Symp Therapeutic Ultrasound*, Seattle, WA, 29 July - 1 August, 2002. University of Washington, Seattle, 2003; pp. 275-281.

Funk, D. "New technology, equipment saved many lives in Iraq", www.tricare.osd.mil/media/Navy-times-article.doc

Holcomb JB , Pusateri AE , Harris RA , Reid TJ , Beall LD, Hess JR, MacPhee M. Dry fibrin sealant dressings reduce blood loss, resuscitation volume, and improve survival in hypothermic coagulopathic swine with grade V liver injuries. J Trauma 1999b; 46: 233-240.

Holcomb JB, Pusateri AE, Harris RA, Charles NC, Gomez RR, Cole JP, Beall LD, Bayer V, MacPhee MJ, Hess JR. Effect of dry fibrin sealant dressings versus gauze packing on blood loss in grade V liver injuries in resuscitated swine. J Trauma 1999a; 46: 49 – 57.

Hoyt DB, Bulger EM, Knudson MM, Morris J, Ierardi R, Sugerman HJ, Shackford SR, Landercasper J, Winchell RJ, Jurkovich G, *et al.* Death in the operating room: an analysis of a multi-center experience. J Trauma 1994: 37: 426-432.

Hwang JJ, Quistgaard J, Souquet J, Crum LA. Portable ultrasound device for battlefield trauma. IEEE Sym. Proceedings 1998; 2: 1663-1666.

Kaczkowski P, Andrew MA, Brayman AA, Kargl SG, Cunitz B, Lafon C, Khokhlova V, Crum LA. *In vitro* examination of non-linear heat deposition in HIFU lesion formation. In : Andrew MA, Crum LA, Vaezy S (eds.) *Proc. 2nd Internat'l Symp Therapeutic Ultrasound*, Seattle, WA, 29 July - 1 August, 2002. University of Washington, Seattle, 2003; pp. 341 - 352.

Martin RW, Vaezy S, Helton S, Caps M, Kaczkowski P, Keilman G, Carter S, Chandler W, Mourad P, Beach K, Crum L. Acoustic liver cauterization: A potential tool for bloodless surgery. Proc. 16th ICA/135th ASA Meeting, Seattle, WA, 2: 721-722, 1998.

Martin RW, Vaezy S, Kaczkowski P, Keilman G, Carter S, Caps M, *et al.* Hemostasis of punctured vessels using Doppler-guided high-intensity ultrasound. Ultrasound Med Biol 1999; 25: 985-990.

Martin RW, Vaezy S, Proctor A, Myntti T, Lee JB, Crum LA. Water-cooled, high-intensity ultrasound surgical applicators with frequency tracking. IEEE Trans Ultrason Ferroelectr Freq Control 2003; 50: 1305-1317.

Patcher HL, Hofsetter SR. The current status of nonoperative management of adult blunt hepatic injuries. Am J Surg 1995; 169: 442-454.

Sauaia A, Moore FA, Moore EE, Moser KS, Brennan R, Read RA, Pons PT. Epidemiology of trauma deaths: a reassessment. J Trauma 1995; 38: 185-193.

Schmiedl UP, Carter S, Martin RW, Eubank W, Winter T, Chang PP, Bauer A, Crum LA. Sonographic detection of acute parenchymal injury in an experimental porcine model of renal hemorrhage: gray-scale imaging using a sonographic contrast agent. AJR Am J Roentgenol 1999; 173:1289-1294.

Shackford SR, Mackersie RC, Holbrook TL, Davis JW, Hollingsworth-Fridlund P, Hoyt DB, Wolf PL. The epidemiology of traumatic death. A population-based analysis. Arch Surg 1993; 128: 571-575.

Vaezy S , Shi X , Martin RW, Chi E, Nelson PI , Bailey MR, Crum LA. Real-time visualization of high-intensity focused ultrasound treatment using ultrasound imaging. Ultrasound Med Biol 2001; 27: 33-42.

Vaezy S, Martin R, Kaczkowski P, Keilman G, Goldman B, Yaziji H, Carter S, Caps M, Crum L. Use of high-intensity focused ultrasound to control bleeding. J Vasc Surg 1999; 29: 533-542.

Vaezy S, Martin R, Schmiedl U, Caps M, Taylor S, Beach K, *et al*. Liver hemostasis using high-

intensity focused ultrasound. Ultrasound Med Biol 1997; 23: 1413-1420.

Vaezy S, Martin R, Yaziji H, Kaczkowski P, Keilman G, Carter S, *et al*. Hemostasis of punctured blood vessels using high-intensity focused ultrasound. Ultrasound Med Biol 1998a; 24: 903-910.

Vaezy S, Martin RW, Kaczkowski P, Keilman G, Carter S, Caps M, Crum LA. Occlusion of blood vessels using high intensity focused ultrasound. Proc. 16th ICA/135th ASA Meeting, Seattle, WA, 2: 1061-1062, 1998b.

Zajtchuk R, Sullivan GR. Battlefield trauma care: Focus on advanced technology. Military Med 1995; 160: 1-7.